

UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
SHERMAN DIVISION

ASSOCIATION FOR MOLECULAR PATHOLOGY, <i>et al.</i> ,)	
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)	
)	Plaintiffs, Case No.: 4:24-CV-824-SDJ
v.)	
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UNITED STATES FOOD AND DRUG ADMINISTRATION, <i>et al.</i> ,)	
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)	
)	Defendants.
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AMERICAN CLINICAL LABORATORY ASSOCIATION, <i>et al.</i> ,)	
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)	
)	Plaintiffs, Case No. 4:24-CV-479-SDJ
v.)	
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UNITED STATES FOOD AND DRUG ADMINISTRATION, <i>et al.</i> ,)	
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)	Defendants.
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**BRIEF OF AMICI CURIAE AMERICAN ASSOCIATION OF BIOANALYSTS,
AMERICAN SOCIETY FOR CLINICAL PATHOLOGY, AMERICAN SOCIETY FOR
MICROBIOLOGY, ASSOCIATION FOR DIAGNOSTICS & LABORATORY
MEDICINE, AND INFECTIOUS DISEASE SOCIETY OF AMERICA IN SUPPORT OF
PLAINTIFFS' MOTIONS FOR SUMMARY JUDGMENT**

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TABLE OF CONTENTS

	Page
IDENTITIES AND INTERESTS OF <i>AMICI CURIAE</i>	1
PRELIMINARY STATEMENT	3
ARGUMENT.....	4
POINT I	4
 CLINICAL LABORATORIES ARE NOT OPERATING OUTSIDE OF THE LAW.....	4
A. Clinical laboratories are regulated under CLIA, an act specifically tailored to the unique nature of LDTs.	5
B. The FDA encourages labs to engage in practices that it has declared unlawful.....	5
POINT II.....	6
 CONSTRUING FDA'S AUTHORITY TO EXTEND TO LDTs WILL HAVE DELETERIOUS EFFECTS ON THE AVAILABILITY OF VITAL TESTS.	6
A. The FDA's guidance on its "enforcement discretion" is inadequate to ensure the continuation of existing LDTs and is already causing serious threats to patient care.....	6
1. The FDA's guidance concerning unmet needs is insufficient to ensure that needed tests will be available.	7
2. The FDA's guidance is inadequate to ensure the continued offering of existing LDTs.....	10
B. The FDA's inflexible process is a poor fit for LDTs and will result in decreased availability of necessary tests, delays in receiving lab results, and increased disparities in access to testing.....	13
1. Labs will stop offering LDTs that cannot justify the costs and regulatory burden of the FDA approval process.	13

2. Laboratories, especially smaller labs and labs focusing on niche specialties, will close.....	14
3. The clinical laboratory industry will experience consolidation leading to greater delays for results and potential bottlenecks.	15
4. There will be significant delays in bringing new LDTs to market.	16
5. Innovation, which is often driven by the development of LDTs, will be reduced.....	16
6. The costs of the Final Rule will fall disproportionately on disadvantaged and underserved populations.	18
7. The Final Rule destabilizes patient care.	19
CONCLUSION	20

IDENTITIES AND INTERESTS OF AMICI CURIAE

Amici Curiae are non-profit associations and societies representing clinical laboratories, laboratory directors, analysts, pathologists, and other physicians and laboratory professionals involved in the development and provision of laboratory-developed tests (“LDTs”).

The **American Association of Bioanalysts**, and its division the National Independent Laboratory Association is a not-for-profit corporation that has represented the clinical laboratory community for over 67 years. It is the principal trade association for community and regional clinical laboratories nationwide.

The **American Society for Clinical Pathology** is the world’s largest professional membership organization for pathologists and laboratory professionals, comprising more than 100,000 anatomic and clinical pathologists, laboratory professionals, residents, and students.

The **American Society for Microbiology** is one of the oldest and largest life science societies with members in the United States and around the world who perform testing for the diagnosis of infectious diseases in clinical, commercial, and public health laboratories

The **Association for Diagnostics & Laboratory Medicine** brings together more than 70,000 clinical laboratory professionals, physicians, research scientists, and business leaders from around the world focused on clinical chemistry, molecular diagnostics, mass spectrometry, translational medicine, lab management, and other areas of progressing laboratory science.

The **Infectious Disease Society of America** represents over 13,000 infectious diseases physicians, scientists and other public health and health care providers specializing in the prevention, diagnosis, and treatment of infectious diseases.

All of the amici share the strong and demonstrable interest in promoting access to high quality laboratory testing which will be harmed by the Final Rule through which FDA has asserted,

despite decades of history and practice to the contrary, the authority to regulate the development and use of LDTs. LDTs are needed by physicians for the prompt and accurate diagnosis of their patients' conditions, often life-threatening.

Amici also believe that the Final Rule, if left unchallenged, will divert limited laboratory resources from the provision of care to new, unnecessary administrative requirements. The additional costs associated with agency oversight will force many laboratories providing LDTs to discontinue this vital patient service, adversely affecting the care provided to a wide spectrum of patient groups, especially in medically underserved populations, who will have less access, or delayed access, to vital tests, including screening and treating newborns for myriad genetic diseases, diagnosing, and ensuring appropriate care for substance abuse victims, and minimizing organ rejection rates for transplant recipients. Amici believe that the effect of the Final Rule will be to stifle the development of new tests to meet future needs, leading to devastating outcomes for patients and the broader public.

Laboratory developed tests are designed and rigorously validated for reliable use in patient care, and physicians have decades of experience relying upon them to diagnose and treat a wide variety of conditions and diseases. They must remain available as a critical tool for physicians to rely upon in clinical and public health settings.

None of the *amici curiae* has any parent corporation or any publicly held corporation that owns 10% or more of its stock. No party's counsel authored this brief in whole or in part. No party or party's counsel and no person other than amici curiae, their members, or their counsel contributed money that was intended to fund preparing or submitting this brief. *Amici Curiae* respectfully submit this Amicus Brief in support of Plaintiffs' motions for summary judgment.

PRELIMINARY STATEMENT

The FDA's final rule on laboratory-developed tests (the "Final Rule") has already had serious detrimental effects on the clinical laboratories that perform these tests, and, ultimately, on the provision of medical care to patients who rely on these tests for prompt diagnosis and treatment.

Prior to the Final Rule, laboratory testing was governed by two complementary regimes working in parallel. Commercially manufactured devices, including prepackaged test kits, were subject to FDA authorization, but once authorized could be mass produced and sold in commerce to clinical laboratories, medical professionals, and even home consumers nationwide.

In contrast, clinical laboratories also offer laboratory developed tests, which are not manufactured products, but rather sets of defined testing procedures that are conducted by skilled laboratory professionals to derive clinical information. LDTs are subject to strict quality assurance and validation requirements as defined in the Clinical Laboratory Improvement Amendments of 1988 ("CLIA"). LDTs offer a level of flexibility and rapid implementation in response to need that is impossible under the FDA's premarket approval process. LDTs are subject to a continual process of refinement and improvement based on feedback from ordering physicians, new peer-reviewed research, improvements in lab techniques or technology, and experience gained from repeatedly conducting a test. Unlike FDA-authorized test kits, the development and roll out of new LDTs is typically measured in weeks or months, as opposed to years.

The FDA seeks to impose the limitations of its process on LDTs — including the immense cost that will make many tests prohibitively expensive to develop and the lengthy approval process that prevents rapid innovation — threatening to destroy the key characteristics that make LDTs an indispensable part of the testing infrastructure.

The FDA asserts that it is only clarifying what the law has always required. According to the FDA, all of the millions of LDTs performed by thousands of clinical laboratories for almost

50 years, have been offered in stark violation of federal law. Only the FDA’s wholly discretionary decision to turn a blind eye — until now — has allowed the industry to flourish in its present form.

But the FDA seeks to forestall the most acute effects of its extreme regulatory overreach — including the serious harms to patients for whom the availability of LDTs is a matter of literal life and death — by announcing that it will continue to tolerate the provision of certain limited categories of nonapproved tests, while reminding laboratories that these offerings violate federal law and that the FDA reserves the right to begin enforcement at any time without further notice.

The Final Rule has already begun to affect the availability of vital LDTs, and this will only become more severe as laboratories are unable to adapt to changing conditions causing the existing pool of LDTs to become outdated and inadequate to serve current needs and as the financial impact of the Final Rule has the predictable effect of causing lab closures and consolidation and the resulting decrease in the availability of vital tests. This Court should rein in the FDA by holding that it has exceeded its statutory authority and has acted arbitrarily and capriciously.

ARGUMENT

POINT I

CLINICAL LABORATORIES ARE NOT OPERATING OUTSIDE OF THE LAW.

According to the FDA, because LDTs are “devices” under the Federal Food, Drug, and Cosmetic Act (“FDCA”), it is only the agency’s “enforcement discretion” that has protected clinical laboratories from bearing the consequences for violating federal law. *See* 89 Fed. Reg. 37,286, 37,295 (May 6, 2024) (“it is illegal to offer [LDTs] without complying with applicable requirements” and “FDA retains discretion to pursue enforcement action for violations of the FD&C Act at any time”). In fact, clinical laboratories are operated by law-abiding professionals in accord with federal law and subject to federal regulators. But the relevant federal law is the

CLIA, administered by the Centers for Medicare & Medicaid Services, not the FDCA.

A. Clinical laboratories are regulated under CLIA, an act specifically tailored to the unique nature of LDTs.

CLIA provides a robust framework for regulating LDTs with a comprehensive approach to quality assurance, flexibility, and continuous improvement. Unlike the FDA's process designed for mass-produced medical devices sold in commerce, CLIA's regulations are tailored to LDTs, which are developed and performed by highly trained and certified professionals.

Under CLIA, developers of LDTs are required to establish performance characteristics of these tests before they are ever offered to patients, and laboratories are required to establish detailed written procedures for all tests, covering everything from specimen collection and handling to result interpretation and reporting. This ensures that each step in the testing process is standardized and rigorously controlled, reducing the likelihood of errors and ensuring that test results are accurate and reliable. By encouraging laboratories to regularly assess and refine their procedures, CLIA fosters an environment where the accuracy and reliability of tests are continually enhanced, while retaining the flexibility needed to rapidly innovate.

The CLIA regulatory process also requires proficiency testing, which involves the regular assessment of a laboratory's ability to perform tests accurately by testing standardized samples and submitting the results for external evaluation. Failure to perform satisfactorily can result in severe penalties, including suspension or revocation of certification, providing a strong incentive for laboratories to maintain the highest quality standards. For over 30 years, this framework has provided a careful balance of oversight and flexibility.

B. The FDA encourages labs to engage in practices that it has declared unlawful.

By asserting that laboratory tests should have been regulated as manufactured medical devices, the FDA effectively declares that laboratories have long been operating outside the

bounds of federal law. Indeed, the FDA’s position is that all laboratory tests developed and used without FDA clearance or approval have been illegally marketed and that the entire laboratory community has been engaged in unlawful practices for decades.

But Congress has repeatedly declined to expand FDA jurisdiction to include LDTs, despite several opportunities to do so. Instead, Congress has consistently affirmed CLIA as the appropriate framework for regulating clinical laboratories and their practices. The FDA’s assertion of authority is an offensive accusation against many thousands of dedicated, highly trained laboratory directors who have diligently followed the rules established by Congress.

The FDA brands an entire industry as lawbreakers and criminals while simultaneously announcing its intention to continue exercising “enforcement discretion,” recognizing that the health care system relies on their continuing to engage in this supposed lawbreaking to forestall dire consequences to the provision of care. *See* 89 Fed. Reg. at 37,293 (“expecting compliance with full QS and premarket review requirements for all currently marketed IVDs offered as LDTs could lead to the loss of access to safe and effective IVDs on which patients currently rely.”) All the while, the FDA continues to hold out the threat of future enforcement.

POINT II

CONSTRUING FDA’S AUTHORITY TO EXTEND TO LDTs WILL HAVE DELETERIOUS EFFECTS ON THE AVAILABILITY OF VITAL TESTS.

The Final Rule infringes upon both the practice of laboratory testing and innovation, as well as upon the practice of medicine by experienced, educated and dedicated medical professionals who need and rely upon such testing. It will have a significant, negative impact on critical patient care services.

A. The FDA’s guidance on its “enforcement discretion” is inadequate to ensure the continuation of existing LDTs and is already causing serious threats to patient care.

In response to concerns raised through the notice and comment process, FDA repeatedly invoked its intention to exercise enforcement discretion to sweep away objections. In reality, this enforcement discretion offers less than it suggests: it ignores the practical realities surrounding the development and modification of tests; it wrongly assumes the testing needs served by laboratories are static and unchanging; it wrongly expects laboratories to indefinitely bear the risk of operating subject to FDA's enforcement discretion; and the narrowness and imprecision of the defined categories undercut its effectiveness.

1. The FDA's guidance concerning unmet needs is insufficient to ensure that needed tests will be available.

In its commentary to the Final Rule, the FDA concedes that "laboratories integrated within a healthcare system may be more likely to stop developing many of these LDTs for unmet needs if the proposed phaseout policy were finalized." 89 Fed. Reg. at 37302. The FDA continues with the following insight: "The cost of compliance with premarket review and QS requirements may be deemed too high given the limited market for many of these LDTs . . . for example, FDA's primary estimates anticipate the cost per premarket submission to range from approximately \$250,000 to \$4.5 million . . . in addition to costs associated with QS requirements, annual reporting requirements (for PMAs) and applicable user fees. . . . [W]e are concerned that many laboratories would stop manufacturing LDTs for unmet needs altogether if they are expected to comply with premarket review and QS requirements." 89 Fed. Reg. at 37302.

The FDA understands that its Final Rule would have a devastating impact upon patient care, but its proposed remedy is not a remedy at all. As the FDA itself repeatedly reminds the public in the commentary to the Final Rule, the exercise of its enforcement discretion is indeed at its discretion. *See, e.g.*, 89 Fed. Reg. at 37297. This means that laboratories, including those within integrated healthcare systems, have no certainty that the investments that they make in their

medically necessary LDTs will survive FDA policies in the coming years. The development of new and updated LDTs under the existing regulatory framework is costly and time-intensive, even absent the additional expense of compliance with the Final Rule. Without assurance that LDTs will be safe from future attempts by the FDA to bring them under its own regulatory framework, laboratories will have difficulty justifying the expenditures required to develop new LDTs or to make medically appropriate modifications to existing LDTs.

Integrated healthcare systems are already struggling to allocate scarce dollars in their laboratory budgets and are making decisions today to shift these dollars from the development and modification of LDTs to other initiatives in light of this uncertainty. The Final Rule's phaseout policy has not yet commenced, yet patient care is already in jeopardy. In addition, because the FDA's announced enforcement discretion extends only to integrated healthcare systems, patients and clinicians of smaller non-affiliated clinics are excluded despite facing the same adverse effects.

The FDA's proposed exercise of enforcement discretion for testing services performed by integrated healthcare system laboratories for unmet needs has the practical effect of replacing the medical judgment of experienced, board-certified physicians with the FDA's determinations of what might or might not fall within an unmet need. Included within the profession of laboratory director under CLIA are board-certified pathologists who are practicing physicians with patient care responsibilities. All laboratory directors, including those licensed to practice medicine and bound by the principles of the Hippocratic Oath, make critical decisions on a continuous basis as to the need for new tests and/or the modification of existing tests to meet patient care needs. Laboratory directors in integrated healthcare systems work hand in hand with the medical staff to prioritize the testing needs of the healthcare system, its patients and its physicians.

However, the commentary to the Final Rule makes very clear that this category of

enforcement discretion is available only for *unmet needs*, without any clear definition or guidelines, and it is unclear how the FDA would assess whether this standard is met. Laboratory Directors operated by integrated healthcare systems have been contacting legal counsel in an attempt to determine their liability if the FDA challenges their medical determinations of “unmet needs”. Some directors have expressed concerns about certifying that an LDT would address an unmet need given the professional and personal risk that they would incur if the FDA disagrees.

At least one integrated healthcare system (a major academic medical center) is considering the termination of its previous plans to bring a vital infectious disease test in-house given the potential risk to its physician laboratory director should the FDA challenge his determination that the test will address an unmet need. The test is used to diagnose critically ill patients in the integrated healthcare system, often in the ICU. The test is available from another reference laboratory, but sending the patient specimens to the other laboratory and waiting for the result generally involves a turnaround time of several days. During this time, the patient’s condition could deteriorate dangerously, or the patient could die. The laboratory director is uncertain if the clear benefit of a rapid turnaround time for a critically ill population fits the FDA’s definition of unmet need and is concerned that he is at risk personally and professionally in the event of a challenge. The commentary to the Final Rule explains that a shorter turnaround time is only eligible as an unmet need “where, due to the circumstances of the patient, the shorter time period to get results is critical for the clinical decisions being made.” 89 Fed. Reg. at 37303. This would mean that the physician laboratory director in this system would need to make a determination for each and every patient as to whether a shorter turnaround time is required, and the FDA could second-guess the director’s medical judgment. This would also result in the same integrated healthcare system having two standards of care, with the “fast” LDT offered to some patients and

the “slow” FDA-authorized test offered to others.

Further, laboratory directors would need to take on the burden of constantly monitoring the industry nationwide to determine whether new tests are available that are “comparable” to an LDT offered to address an unmet need, because the appearance of any FDA-authorized test in the marketplace may require laboratories to immediately cease offering LDTs. Incredibly, the FDA states in the commentary to the Final Rule that “improvements in performance or lower cost in comparison to an FDA-authorized IVD that meets the patient’s needs does not fall within this [category of enforcement discretion].” 89 Fed. Reg. at 37303. Even if a board-certified laboratory director makes a medical determination that an LDT has improved performance over the FDA-authorized test, the FDA takes the position that it can require that physician to utilize a poorer performing test. This is an unacceptable infringement upon the practice of medicine.

2. The FDA’s guidance is inadequate to ensure the continued offering of existing LDTs.

The FDA recognizes that the application of the Final Rule to existing LDTs will have detrimental results, including “prompt[ing] many laboratories to stop offering tests even if they are safe and effective,” and causing the closure of laboratories — “particularly small laboratories” — unable to shoulder the compliance burden. 89 Fed. Reg. at 37304. The FDA addresses this problem by announcing its intention to exercise discretion not to enforce its authority over existing LDTs, provided they are not subject to any “major change or modification.”

But to the extent that this exercise of enforcement discretion responds to the identified harms, it is only a partial fix that forestalls the harm without preventing it. The needs served by LDTs are not static. For example, LDTs currently serve a vital role in monitoring and treating infectious disease outbreaks. As new pathogens are identified and existing diseases mutate and evolve, LDTs are rapidly developed to detect novel strains. The menu of LDTs for infectious

diseases in existence now is not likely to be adequate to respond to the *next* outbreak. For example, with antimicrobial resistance on the rise globally, new assays will need to be rapidly developed to guide appropriate antimicrobial therapy. And as the number of immunocompromised patients increases, so does the need for testing of pathogens that predominately impact these susceptible populations. This will be disproportionately addressed by LDTs as the volume of testing would not be sufficient to financially justify seeking FDA authorization.

Similarly, LDTs are essential to identifying new drugs leading to overdoses. As traffickers introduce novel substances into the illicit drug pipeline, LDTs are rapidly developed and deployed to detect new analytes. LDTs are critical in detecting synthetic fentanyl and other new drugs fueling the opioid epidemic — substances not detectable with FDA-cleared test kits. In the case of overdose or other adverse reaction, accurate identification of the substances involved is essential to effective treatment. A menu of LDTs designed to detect only substances currently in circulation will be inadequate to respond to future innovation in the illicit drug trade. Prior to the Final Rule, as new drug substances were identified, they were rapidly added (after validation under CLIA) to existing LDTs. Under the Final Rule, such additions would be impossible in a timeframe that would keep the test relevant to patient care.

Other LDTs are modified in response to changes in the state of medical knowledge. For example, genetic tests are employed to make predictive determinations about susceptibility to disease or responsiveness to treatment. When peer-reviewed research identifies new genetic markers that improve predictive accuracy, LDTs can be rapidly updated to detect them, providing better information to treating physicians. Under the Final Rule, physicians will be forced to rely on increasingly outdated tests, effectively freezing the state of knowledge for many purposes.

The FDA is aware that limiting its exercise of enforcement discretion to currently existing

LDTs provides only a limited patch, noting that “[a]s IVDs evolve, compliance with premarket review and QS requirements will be phased in according to the natural lifecycle of test development and use.” 89 Fed. Reg. at 37304. And the critical care needs that the FDA identifies in justifying its exercise of discretion apply equally to patients who require monitoring via newly developed tests that were not already in existence and are therefore not eligible for enforcement discretion. 89 Fed. Reg. at 37305. To the FDA, the impact on future patients is apparently out of sight, out of mind. And the negative impacts will be just as real and destructive if they phase in more gradually as demand shifts to newer tests.

The Final Rule is already having real world effects. For example, one laboratory developed a new LDT providing superior detection of Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS) over existing tests. These “forever chemicals” are a major public health concern. But because this test was not validated until after the issuance of the Final Rule, the lab is able to offer only a prior, inferior version of the test today and must wait to implement the more relevant test. As new PFAS are identified, existing tests will become increasingly outdated.

Finally, as a result of the narrow limits of this enforcement discretion, LDTs may become unavailable for reasons beyond the laboratory’s control. Sometimes a test becomes impossible to conduct as designed. For example, shortages or supply chain problems may require sourcing a particular reagent or collection device from a different vendor or substituting a different chemical in its place. Similarly, the failure of older lab equipment for which replacement parts are no longer available may require the substitution of new equipment. Prior to the Final Rule, a laboratory could respond to such circumstances by making necessary modifications and then revalidating the test. Now, to the extent such modifications amount to a “major change” — a threshold that the FDA’s guidance leaves vague — the lab will be forced to discontinue offering the LDT entirely.

B. The FDA's inflexible process is a poor fit for LDTs and will result in decreased availability of necessary tests, delays in receiving lab results, and increased disparities in access to testing.

The FDA's exercise of enforcement discretion is at best a partial, temporary fix for a limited universe of LDTs. Tests that do not fit within the FDA's narrow parameters for enforcement discretion will be available only after receiving FDA authorization. The effects of the Final Rule on the timely availability of tests and ultimately on patient care are predictable.

1. Labs will stop offering LDTs that cannot justify the costs and regulatory burden of the FDA approval process.

The Final Rule introduces a costly dual regulatory framework, requiring LDTs to meet both FDA and CLIA standards. This will impose substantial financial and administrative burdens on laboratories, many of which will lack the resources to comply. By one estimate, the rule could cost the laboratory industry up to \$50 billion over five years, with these costs potentially being passed on to healthcare providers and patients. Smaller laboratories, hospitals, and community testing facilities, which often operate with limited budgets and thin financial margins, could be forced to reduce or eliminate LDT offerings, reducing patient access to vital diagnostic tests.

The FDA estimates an average cost of premarket submission exceeding \$3 million dollars per test, not including ongoing compliance costs. 89 Fed. Reg. at 37302, 37304. Some labs currently offer a menu of thousands of LDTs and may develop hundreds of new LDTs each year — for example, one laboratory tests for approximately 450 specific analytes in various combinations in over 2,000 toxicology-based LDTs. The cost of submitting all new tests for FDA review would be prohibitively expensive, with the predictable result that esoteric tests for less common conditions will no longer be financially viable. Labs will focus their resources on a smaller number of more common conditions where higher testing volume will allow them to recoup their costs.

For example, due to the smaller population size and the unique aspects of pediatric care,

commercial companies often do not prioritize developing FDA-authorized tests for pediatric diseases. LDTs fill this gap by providing tailored diagnostic tools for children. Imposing the costs of the FDA's process on LDTs will create a similar barrier to the creation of new pediatric LDTs. Tests for serious but less common infectious diseases will be similarly affected. The relative infrequency of testing for some diseases will mean that clearance by the FDA is not fiscally viable.

Other tests, such as the therapeutic drug monitoring for pyrimethamine — a necessary test to prevent toxicity in patients with certain parasitic infections — are not profitable and are effectively cross-subsidized by other tests conducted at the same lab. Under the new rule, the high costs associated with the FDA approval process would prevent the creation of such infrequently run tests. In the case of the test for pyrimethamine, which is only available from a single U.S. laboratory, discontinuation due to the prohibitive cost would result in complete loss of access to crucial testing, likely resulting in increased mortality.

2. Laboratories, especially smaller labs and labs focusing on niche specialties, will close.

While some labs may be able to survive on the remaining revenues from a reduced menu of LDTs, others — including many smaller and specialty laboratories — will not. Few individual LDTs produce revenue sufficient to justify the cost of FDA approval, and many labs may no longer be financially viable with significantly reduced test offerings. This will disproportionately affect rural areas, some of which are likely to be left without a single local clinical laboratory.

Many specialty labs currently offer a large menu of niche LDTs, few of which individually bring in significant revenue. For example, one clinical laboratory that specializes in allergy testing offers a menu of LDTs covering a broad array of allergens, and, prior to the Final Rule, regularly added LDTs for new allergens to assist in diagnosing more unusual allergic reactions. Following the issuance of the Final Rule and the effective freezing of its menu of offerings, this laboratory's

continued financial viability is in doubt. When a specialty lab closes, the result will often be the complete disappearance of certain tests from the market. The revenue impact due to loss of jobs and tax revenue to communities where such laboratories exist will be substantial.

3. The clinical laboratory industry will experience consolidation leading to greater delays for results and potential bottlenecks.

The closure of some labs and the decreased LDT offerings by others will result in an increased concentration of testing in a smaller number of laboratories, leading to delays in lab results as samples increasingly need to be sent out for testing. This effect will be most pernicious for laboratories attached to hospitals, where rapid turnaround is essential to inform diagnosis and treatment. Due to the need to ship samples out, results that could previously be returned in hours from a hospital lab will now take at least a day — a delay that could be critical in many situations.

For example, therapeutic drug monitoring is often performed using LDTs to ensure proper dosing of medications like immunosuppressive drugs. Delays in testing could result in adverse patient outcomes, including organ rejection in transplant patients. Delayed results can also have severe consequences for conditions requiring rapid diagnosis and treatment, like meningitis, encephalitis, or sepsis. Accurate treatment for bacterial meningitis depends on rapid diagnosis and antimicrobial susceptibility testing, both areas where LDTs are vital. Any delays could lead to inappropriate treatment, worsened patient outcomes, and increased risk of antimicrobial resistance.

Rapid results are also critical for urgent pediatric care. For example, newborn screening tests for genetic and metabolic disorders, which are all LDTs, require rapid turnaround to diagnose and treat newborns effectively. Any delays in these processes could exacerbate genetic/metabolic disorders in newborns, leading to worse health outcomes.

The consolidation of the lab industry and concentration of particular LDTs in a small number of locations creates an increased risk of delays due to congestion. If, for example, a disease

outbreak or environmental contamination results in a spike in demand for a particular LDT, the small number of labs offering that test may be unable to absorb the demand, leading to backlogs, lengthy delays, and a greater risk of single points of failure. Where one lab is the only provider of a test in an entire region, a problem at that lab — *e.g.*, equipment failure, staffing shortages, or weather emergency — could temporarily result in the complete unavailability of certain tests.

4. There will be significant delays in bringing new LDTs to market.

Prior to the Final Rule, many clinical labs could develop and validate a brand new LDT in 30–60 days or less. FDA approval can currently take at least six to nine months, without accounting for anticipated slowdowns due to the enormous increase in volume of applications under the Final Rule. While the FDA has historically approved fewer than 100 diagnostic devices per year, estimates suggest as many as 160,000 LDTs in existence. The proposed rule would create bottlenecks in the approval process, not only delaying the availability of LDTs but also impacting the FDA’s ability to review other medical devices, further exacerbating delays in patient care.

The quick turnaround possible under CLIA is critical to dealing with rapidly developing situations like infectious disease outbreaks or toxicology where the FDA’s lengthy process may render some tests obsolete by the time they are approved. But delay is significant even for more routine testing. Some LDTs are developed in collaboration with treating physicians for the diagnosis or treatment of particular patients. A six-month delay in the availability of a needed test could have a substantial impact on quality of life or success of treatment.

5. Innovation, which is often driven by the development of LDTs, will be reduced.

LDTs have historically driven much innovation in medical testing. The Final Rule, by imposing substantial burdens on the development of new tests, is likely to curtail this innovation. Hospitals often create tests to address immediate clinical needs or to improve existing diagnostic

tests based on the latest research. For example, many laboratories modify FDA-authorized assays to better serve their patient populations, such as using alternative transport media or clinically relevant sample types. FDA-authorized test kits are often not validated for pediatric use or lack pediatric reference ranges. LDTs allow pediatric hospitals to modify these tests to ensure they are appropriate for children, such as using smaller sample volumes or adjusting reference intervals for different stages of child development. LDTs have been vital in diagnosing and managing pediatric cancers, such as leukemia and lymphoma, where timely and accurate diagnostics are critical.

Numerous existing LDTs measure or detect analytes for which an FDA-authorized test kit has never been available. For example, laboratories have developed LDTs to detect more than 400 different allergens, most of which are not available from IVD manufacturers. Without the ability to inexpensively innovate, laboratories may not be able to provide new diagnostic tools essential for patient care, especially in specialized fields like allergy detection and orphan diseases. LDTs have also been employed to provide broad molecular profiling in oncology. For example, next-generation sequencing (NGS) tests are not typically available in pre-packaged, FDA-authorized kits but are essential for personalized cancer treatment.

LDTs were also rapidly developed during the COVID-19 pandemic to meet the urgent need for accurate testing. They are similarly essential for rapid diagnostics for mosquito-borne diseases like dengue or West Nile virus. During the 2022 Mpox outbreak, LDTs were among the first tests available, playing a crucial role in early detection and management. LDTs allow laboratories to quickly develop and modify tests in response to new information, such as changes in a pathogen's genetic makeup or transmission patterns. Indeed, many infectious disease LDTs are considered the standard of care, with years of clinical experience, peer-reviewed literature and clinical guidelines supporting their safety, efficacy and use.

This flexibility is crucial for addressing unique health needs in diverse populations. For example, some LDTs are specifically designed to account for genetic differences that affect drug metabolism and treatment efficacy across different ethnic groups. The FDA's rule would hinder the ability to innovate and customize tests that cater to the specific needs of different communities, thereby reducing the quality and personalization of care available to these populations.

6. The costs of the Final Rule will fall disproportionately on disadvantaged and underserved populations.

The substantial costs of the Final Rule will fall most heavily on already disadvantaged and underserved populations, such as those in rural areas, low-income communities, and historically underserved racial and ethnic groups. Many of these populations rely on local laboratories for essential diagnostic services, including LDTs tailored to specific regional health needs. For example, Indigenous American populations in Arizona and New Mexico are at high risk for diseases like Hantavirus and Coccidioidomycosis, which require rapid diagnosis but have no FDA-authorized molecular or antigen assays available. The Final Rule could force local laboratories to halt their LDT offerings due to the prohibitive costs and resource demands, thereby reducing access to timely and necessary diagnostics for these vulnerable communities.

Many rural communities are served by smaller laboratories that would struggle to meet the new requirements and are thus more likely to close or drastically reduce testing services. This would limit access to tests in areas that already face significant healthcare challenges and may require patients to travel long distances to access testing, delaying diagnosis and treatment.

Higher compliance costs will lead to increased prices for diagnostic tests or reduced availability, disproportionately affecting economically and racially marginalized communities. Indeed, the FDA's own analysis acknowledges that vulnerable populations relying on LDTs for diagnostic testing may face decreased access to these tests if the rule is implemented.

The Final Rule will also disproportionately affect particularly vulnerable patient populations, like children. Many pediatric patients rely on LDTs for specialized care not available through commercial tests. Pediatric specialty care often relies on LDTs to provide accurate and timely diagnostics for conditions like perinatal infections or genetic disorders. Without these tests, children with complex health needs may face delayed diagnoses and treatment, requiring them to travel long distances to specialized centers, increasing stress and burden on their families.

7. The Final Rule destabilizes patient care.

As noted above, the FDA's mixed messages about its enforcement discretion has thrown the clinical laboratory field into a state of confusion. But the uncertainty created by the FDA goes further — for example, casting doubt on the longstanding use of digital pathology. Traditionally, pathologists (physicians trained in anatomic and clinical pathology who are primarily responsible for the diagnosis of diseases such as cancer) examine glass slides that contain thin sections of biopsy specimens. After examination, pathologists render their medical diagnoses. In digital pathology, the glass slides are scanned for the pathologist to review, in lieu of or in addition to the glass slides, allowing them to rapidly render a diagnosis despite not being at the same location. The process is analogous to how most radiology images are reviewed today: images are sent digitally to radiologists, who then examine them on a monitor and issue their interpretations.

The United States is facing its most dire shortage of pathologists in a generation, particularly among those with sub-specialty expertise. As with shortages in other specialties, rural and economically disadvantaged communities are most affected. Because pathologists are primarily responsible for the pathological diagnosis of disease, lack of access to pathology expertise has a direct and negative impact upon patient care. For at least two decades, the use of digital pathology has alleviated the patient care jeopardy created by scarce pathologist resources, enabling pathologists to review slides and issue their professional medical interpretive reports on

a timely basis. While it is theoretically possible to ship glass slides across the country to the interpreting pathologist, as a practical matter, shipping slides delays the interpretations for at least several days, and the slides themselves are subject to damage or destruction.

From a medical standpoint, the review of a glass slide and the review of a digital image of a glass slide are interchangeable. Digital pathology simply supports the pathologist's practice of medicine. The FDA has never exerted authority over the pathologist's review of glass slides, presumably because it does not have the authority to regulate the practice of medicine. And there is no test result or written report or any other type of test analysis generated by the *scanning* of a glass slide. The only result is the medical interpretive report issued by the pathologist, and this report is unquestionably a professional physician service outside the purview of the FDA. Glass slides and digital images of slides are not laboratory tests, and therefore cannot be LDTs.

However, the FDA's commentary in the Final Rule indicating that it intends to regulate digital pathology has thrown the field into chaos. *See* 89 Fed. Reg. at 37312. This is a bizarre position, as the FDA does not regulate the production or review of glass slides, but purports to have the authority to subject digitally scanned slides to the Final Rule.

Due to this threatened exercise of authority and the high cost of compliance with the Final Rule, pathology practices and laboratories across the country are hesitating to make investments in digital pathology. Decisions to utilize digital pathology traditionally have fallen within the practice of medicine. The effect of the FDA's overreach is that pathologists (medical doctors) now have a strong disincentive to integrate digital pathology into their medical practice, and patients will suffer from the lack of access to and/or delayed access to pathology expertise.

CONCLUSION

For the foregoing reasons, and those stated in the Briefs of Plaintiffs ACLA and AMP, *Amici Curiae* request that the Court grant Plaintiffs' motions for summary judgment.

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CERTIFICATE OF SERVICE

I hereby certify that, on October 7, 2024, a true and correct copy of the above and foregoing document was served on all parties that have appeared through the Court's electronic filing system as of the time of filing.

By: /s/ Michael Y. Hawrylchak
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